FILE 'CAPLUS, MEDLINE, BIOSIS, CA, SCISEARCH, EMBASE' ENTERED AT 15:30:16
ON 18 NOV 2004

L1	16	S BLUM RICHARD/AU
L2	8	DUPLICATE REM L1 (8 DUPLICATES REMOVED)
L3	0	S BLUM S RICHARD/AU
L4	0	S BLUM RICARD/AU
L5	6	S RICARD-BLUM
L6	2	DUPLICATE REM L5 (4 DUPLICATES REMOVED)
L7	0	S RICARD-BLUM/AU
L8	7169	S PYRIDINOLINE
L9	110364	S SYNOVIA OR SYNOVIAL OR SYNOVIUM
L10	160	S L8 AND L9
L11	83	S L8 (S) L9
L12	32	DUPLICATE REM L11 (51 DUPLICATES REMOVED)

L12 ANSWER 30 OF 32 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 21

TI ASSAY OF PYRIDINIUM CROSS-LINKS IN SERUM USING NARROW-BORE ION-PAIRED REVERSED-PHASE HIGH-PERFORMANCE LIQUID-CHROMATOGRAPHY

AB The pyridinium crosslinks are important biomarkers of mature hard tissue collagen degradation. This paper describes an isocratic ion-paired reversed-phase high-performance chromatographic assay using narrow-bore columns and high-sensitivity fluorescence detection to enable for the first time the determination of pyridinium crosslinks in both serum and **synovial** fluid samples. Extracted freeze-dried acid hydrolysates were re-suspended in 20 mM pentafluoropropionic acid (PFPA). Separations were carried out using an Exsil 100 5-mum ODS2 column (100 mm x 2.1 mm I.D.) eluted with 10 mM PFPA in water at 0. 1 5 ml/min and detected using a Jasco 821-FP detector (xenon lamp: excitation 290 nm, emission 400 nm). Fluorescent response was linear from 269 to 8620 fmol for **pyridinoline** (Pyr) and 85 to 2710 fmol for deoxypyridinoline (dPyr). The limits of detection were 28 and 57 fmol, respectively. The coefficient of variation for extraction and analysis of normal serum was 7.96% for Pyr and 6.30% for dPyr (n = 6). The mean +/- S.D. concentration of Pyr in normal serum was 3.26 +/- 0.83 nM.

SO JOURNAL OF CHROMATOGRAPHY-BIOMEDICAL APPLICATIONS, (29 JAN 1993) Vol. 612, No. 1, pp. 41-48.
ISSN: 0378-4347.

AU JAMES I (Reprint); CROWLEY C; PERRETT D

L5 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

TI Hydroxypyridinium collagen crosslinks in serum, urine, synovial fluid and synovial tissue in patients with rheumatoid arthritis compared with osteoarthritis

AB Objective. To investigate the relationship between inflammation markers and content of pyridinium crosslinks in hydrolyzates of **synovial** tissue and to specify the significance of urinary excreted **pyridinoline**, released primarily from collagen I and II of bone and cartilage, and deoxypyridinoline released esp. from collagen I of bone and dentin, dependent on **disease** activity in rheumatoid arthritis (RA). Methods. Synovial tissue and fluid from knee endoprosthesis surgery, as well as simultaneously obtained serum and urine, were collected from 12 patients with inactive RA or RA with low **disease** activity [iRA: C-reactive protein (CRP) <28 mg/l], 10 with active RA (aRA: CRP .gtoreq.28 mg/l) and 21 with OA. After prepn. of the **synovial** tissue, including hydrolysis, completely released **synovial pyridinoline** and deoxypyridinoline crosslinks as well as those from **synovial** fluid, serum and urine were investigated using a gradient ion-paired reversed-phase HPLC method. Crosslink levels in synovial tissue are expressed as mol/mol collagen, assuming 300 residues of hydroxyproline per collagen mol., also measured by HPLC. Results. In the **synovial** tissue of aRA patients we found significantly elevated total **pyridinoline** concns. and **pyridinoline**/deoxypyridinoline (Pyr/Dpyr) quotients compared with the iRA and OA controls, indicating an elevated crosslinking d. of mature **synovial** tissue collagen with increased activity of RA. Pyridinoline levels and the Pyr/Dpyr ratio were correlated with those of urine and with acute-phase reactants in RA patients. Compared with serum crosslink levels, which were unrelated to **disease** activity, the urinary concn. of pyridinoline was increased by a factor of 2 and showed a simultaneous increase with increasing synovitis. Conclusion. Both crosslinking d. and degrdn. of mature collagen from synovial tissue depend on the **disease** activity in RA. Urinary excretion of assocd. crosslinks, expressed as the Pyr/Dpyr ratio, correlates with those in synovial tissue and may be confirmed as a marker of synovial tissue collagen degrdn. We suggest that increased crosslinking of mature collagen in the synovial tissue of RA is related to an inflammation-dependent regulation of collagen synthesis in activated synovial fibroblasts, in which lysyl oxidase represents the final enzymic step for crosslinking.

SO Rheumatology (Oxford, United Kingdom) (2003), 42(2), 314-320
CODEN: RUMAFK; ISSN: 1462-0324

AU Kaufmann, J.; Mueller, A.; Voigt, A.; Carl, H. D.; Gursche, A.; Zacher, J.; Stein, G.; Hein, G.

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SO Rheumatology (Oxford, United Kingdom) (2003), 42(2), 314-320
CODEN: RUMAFK; ISSN: 1462-0324

AU Kaufmann, J.; Mueller, A.; Voigt, A.; Carl, H. D.; Gursche, A.; Zacher, J.; Stein, G.; Hein, G.

L5 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

TI Association of baseline levels of urinary glucosyl-galactosyl-pyridinoline and type II collagen C-telopeptide with progression of joint destruction in patients with early rheumatoid arthritis

AB Objective. To evaluate whether measurements of urinary glucosyl-galactosyl-**pyridinoline** (Glc-Gal-PYD) and urinary C-terminal crosslinking telopeptide of type II collagen (CTX-II), 2 new markers of destruction of the **synovium** and cartilage collagen breakdown, resp., are assocd. with the progression of joint damage in patients with early rheumatoid arthritis (RA), and to compare this assocn. with that with serum matrix metalloproteinase 3 (MMP-3), a proteinase expressed by **synovial** tissue and chondrocytes, and that with serum C-reactive protein (CRP), an index of systemic inflammation. Methods. The prospective study cohort comprised 116 patients with early RA who were part of a large, double-blind, randomized study comparing the efficacy of etanercept and methotrexate. The relationship between baseline levels of urinary Glc-Gal-PYD, urinary CTX-II, and serum MMP-3 and the progression of joint destruction, as measured by changes in the modified Sharp score (av. findings of 2 independent readers) over 1 yr, was investigated. Results. Levels of urinary Glc-Gal-PYD (+70%), urinary CTX-II (+104%), and serum MMP-3 (+219%) were elevated compared with the levels in 76 healthy controls. The baseline levels of Glc-Gal-PYD (r = 0.30), CTX-II (r = 0.25), and MMP-3 (r = 0.29) correlated with the changes over 1 yr in the total Sharp score (joint space narrowing and bone erosion). Patients with baseline levels of Glc-Gal-PYD, CTX-II, and MMP-3 that were higher than the mean + 2 SD in healthy controls had a significantly greater progression of joint damage, with an increase in the total Sharp score over 1 yr that was from 3- to 8-fold higher than that in patients with low baseline levels of these markers. Moreover, patients

with these higher levels of Glc-Gal-PYD, CTX-II, and MMP-3 had a higher risk of progression of the **disease** (increase in total Sharp score .gtoreq.0.5 units) than did the other patients (relative risks and 95% confidence intervals [95% CI] 3.3 [95% CI 1.5-7.4], 2.5 [95% CI 1.1-5.7], and 2.5 [95% CI 1.1-5.6], resp.). The baseline serum level of CRP was not significantly assocd. with the progression of joint damage. Adjustment of the levels of Glc-Gal-PYD, CTX-II, and MMP-3 according to radiol. damage at baseline did not alter their assocn. with progression. After adjustment for serum CRP, the relative risk slightly decreased, but remained significant, for Glc-Gal-PYD (2.6 [95% CI 1.1-6.3]). Patients with both increased levels of the mol. markers and radiol. damage at baseline had a higher risk of progression of joint damage than did those with either high mol. marker levels or radiol. damage. Conclusion. High baseline levels of Glc-Gal-PYD, CTX-II, and MMP-3 are assocd. with increased risk of progression of joint destruction over 1 yr in early RA. The assocn. between baseline levels of urinary Glc-Gal-PYD and progression of joint erosion was independent of the severity of radiol. damage and inflammation at baseline. Combining the measurements of these mol. markers with radiol. assessment of joint damage may be useful for identifying patients with RA who are at high risk of rapid progression and for whom early aggressive treatment would be beneficial.

SO Arthritis & Rheumatism (2002), 46(1), 21-30
CODEN: ARHEAW; ISSN: 0004-3591

AU Garnero, Patrick; Gineyts, Evelyne; Christgau, Stephan; Finck, Barbara; Delmas, Pierre D.

L5 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

TI Cross sectional evaluation of biochemical markers of bone, cartilage, and synovial tissue metabolism in patients with knee osteoarthritis: Relations with **disease** activity and joint damage

AB To analyze the relations between the urinary levels of type II collagen C-telopeptide (CTX-II) and glucosylgalactosyl **pyridinoline** (Glc-Gal-PYD)-two newly developed biochem. markers of type II collagen and **synovial** tissue destruction resp.-**disease** activity and the severity of joint destruction in patients with knee osteoarthritis (OA). The clin. performance of these two new markers was compared with that of a panel of other established biochem. markers of connective tissue metab. The following biochem. markers were measured in a group of 67 patients with knee OA (mean age 64 yr, median **disease** duration eight years) and in 67 healthy controls: for bone, serum osteocalcin, serum and urinary C-telopeptide of type I collagen (CTX-I); for cartilage, urinary CTX-II, serum cartilage oligomeric matrix protein (COMP), and serum human cartilage glycoprotein 39 (YKL-40); for synovium, urinary Glc-Gal-PYD, serum type III collagen N-propeptide (PIIINP), serum hyaluronic acid (HA); and for inflammation, serum C reactive protein. Biochem. markers were correlated with pain and phys. function (WOMAC index) and with quant. radiog. evaluation of the joint space using the posteroanterior view of the knees flexed at 30.degree.. All bone turnover markers were decreased in patients with knee OA compared with controls (-36%, -38%, and -52%, $p<0.0001$ for serum osteocalcin, serum CTX-I and urinary CTX-I, resp.). Serum COMP (+16%, $p=0.0004$), urinary CTX-II (+25%, $p=0.0009$), urinary Glc-Gal-PYD (+18%, $p=0.028$), serum PIIINP (+33%, $p<0.0001$), and serum HA (+ 233%, $p<0.0001$) were increased. By univariate analyses, increased urinary Glc-Gal-PYD ($r=0.41$, $p=0.002$) and decreased serum osteocalcin ($r=-0.30$, $p=0.025$) were assocd. with a higher total WOMAC index. Increased urinary CTX-II ($r=-0.40$, $p=0.0002$) and Glc-Gal-PYD ($r=-0.30$, $p=0.0046$) and serum PIIINP ($r=-0.29$, $p=0.0034$) were the only markers which correlated with joint surface area. By multivariate analyses, urinary Glc-Gal-PYD and CTX-II were the most important predictors of the WOMAC index and joint damage, resp. Knee OA appears to be characterized by a systemic decrease of bone turnover and increased cartilage and synovial tissue turnover. CTX-II, Glc-Gal-PYD, and PIIINP may be useful markers of **disease** severity in patients with knee OA.

SO Annals of the Rheumatic Diseases (2001), 60(6), 619-626
CODEN: ARDIAO; ISSN: 0003-4967

AU Garnero, P.; Piperno, M.; Gineyts, E.; Christgau, S.; Delmas, P. D.; Vignon, E.

ANSWER 4 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

TI Urinary excretion of glucosyl-galactosyl **pyridinoline**: a specific biochemical marker of **synovium** degradation

AB Glucosyl-galactosyl pyridinoline (Glc-Gal-PYD), which has been identified in urine, is a glycosylated analog of pyridinoline. The tissue distribution of this mol. has not been yet detd. and its utility as a potential biochem. marker of joint degrdn. in patients with joint diseases has not been investigated. In this study, we demonstrate that Glc-Gal-PYD is abundant in human synovium tissue, absent from bone and present in minute amts. in cartilage and other soft tissues, such as muscle and liver. Using an ex vivo model of human joint tissue degrdn., we found that Glc-Gal-PYD is released from synovium tissue, but not from bone and cartilage. The urinary level of Glc-Gal-PYD was increased by 109% in patients with rheumatoid arthritis (RA) compared with healthy adults, but was normal in patients with Paget's **disease** of bone. In addn., Glc-Gal-PYD was higher in those patients with destructive **disease**, as assessed by X-rays of the joints, than in those with non-destructive RA. Glc-Gal-PYD may be useful for the clin. investigation of patients with joint **disease**.

SO Rheumatology (Oxford, United Kingdom) (2001), 40(3), 315-323
CODEN: RUMAFK; ISSN: 1462-0324

AU Gineyts, E.; Garnero, P.; Delmas, P. D.

L5 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

TI Methods and kits for diagnosing or monitoring a synovial or osteoarticular pathology comprising the use of a specific marker of the synovial tissue degradation

AB The invention concerns a method for diagnosing and monitoring the evolution of a synovial pathol. characterized in that it consists in: (i) contacting in vitro a biol. sample from an individual with means for measuring a synovial pathol.-specific marker; (ii) detg. the specific marker level; (iii) optionally comparing the marker level with a ref. level representing the absence of pathol. or representing a predetd. stage of the pathol., the marker level relative to the ref. level indicating the presence or evolution of the synovial pathol. Synavial collagen degrdn. markers are pyridinoline biglycans; they are detected by immunoassays, chromatog. methods, fluorometry etc. As ref. material creatinine is used.

SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2

IN Delmas, Pierre; Garnero, Patrick; Gineyts, Evelyne